PATENT COOPERATION TREATY

SEP 26 2008

From the INTERNATIONAL SEARCHING AUTHORITY

To: WILLIAM GEARY
NUTTER MCCLENNEN & FISH LLP
WORLD TRADE CENTER WEST
155 SEAPORT BOULEVARD
BOSTON, MA 02210-2604

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing *(day/month/year)*	23 SEP 2008
Applicant's or agent's file reference 107568-0005	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US2008/064481	International filing date *(day/month/year)* 22 May 2008
Applicant JOHNSON & JOHNSON REGENERATIVE THERAPEUTICS, LLC	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35

   For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, within **20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450	Authorized officer: Blaine R. Copenheaver
Facsimile No. 571-273-3201	Telephone No. 571-272-7774

Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

Nutter McClennen & Fish LLP
IP Docketing Department

Client / Matter: 107568-0005
Action Type: Search / Written Opinion
~~Action~~ ISR Due: 11/23/08 Final WO Deadline 12/23/08
Docketed by: ejc Date: 9/26/08

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: WILLIAM GEARY
NUTTER MCCLENNEN & FISH LLP
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155 SEAPORT BOULEVARD
BOSTON, MA 02210-2604

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(PCT Rule 44.1)

	Date of mailing *(day/month/year)* 23 SEP 2008
Applicant's or agent's file reference 107568-0005	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US2008/064481	International filing date *(day/month/year)* 22 May 2008
Applicant JOHNSON & JOHNSON REGENERATIVE THERAPEUTICS, LLC	

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   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

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   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, within **20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver Telephone No. 571-272-7774

Form PCT/ISA/220 (January 2004) *(See notes on accompanying sheet)*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 107568-0005	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US2008/064481	International filing date *(day/month/year)* 22 May 2008	(Earliest) Priority Date *(day/month/year)* 01 June 2007
Applicant JOHNSON & JOHNSON REGENERATIVE THERAPEUTICS, LLC		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

   b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No. III)

4. With regard to the **title**,

   ☒ the text is approved as submitted by the applicant

   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   ☒ the text is approved as submitted by the applicant

   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

   a. the figure of the drawings to be published with the abstract is Figure No. 1B

   ☐ as suggested by the applicant

   ☒ as selected by this Authority, because the applicant failed to suggest a figure

   ☐ as selected by this Authority, because this figure better characterizes the invention

   b. ☐ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/064481

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 9/00 (2008.04)
USPC - 424/424
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61K 9/00 (2008.04)
USPC - 424/400, 422, 423, 424, 425, 426

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, Google Scholar

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/0064088 A1 (CARVALHO et al) 03 April 2003 (03.04.2003) entire document	1-20
Y	US 2006/0292131 A1 (BINETTE et al) 28 December 2006 (28.12.2006) entire document	1-20
Y	US 5,980,508 A (CARDAMONE et al) 09 November 1999 (09.11.1999) entire document	7-12
Y	US 4,373,527 A (FISCHELL) 15 February 1983 (15.02.1983) entire document	14, 15, 17

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 August 2008	23 SEP 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: WILLIAM GEARY
NUTTER MCCLENNEN & FISH LLP
WORLD TRADE CENTER WEST
155 SEAPORT BOULEVARD
BOSTON, MA 02210-2604

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	23 SEP 2008
Applicant's or agent's file reference 107568-0005	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2008/064481	22 May 2008	01 June 2007

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - A61K 9/00 (2008.04)
USPC - 424/424

Applicant
JOHNSON & JOHNSON REGENERATIVE THERAPEUTICS, LLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	20 August 2008	Blaine Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/237 (cover sheet) (April 2007)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2008/064481

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing

      ☐ contained in the international application as filed

      ☐ filed together with the international application in electronic form

      ☐ furnished subsequently to this Authority for the purposes of search

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2008/064481

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-22	YES
	Claims	None	NO
Inventive step (IS)	Claims	None	YES
	Claims	1-22	NO
Industrial applicability (IA)	Claims	1-22	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1-6, 13, 16, and 18 lack inventive step under PCT Article 33(3) as being obvious over Carvalho et al. in view of Binette et al.

Regarding claim 1, Carvalho et al. disclose a delivery device (Abstract, surgically implanted delivery device for therapeutic agents) comprising a housing having a cell chamber (Para. [0067] implantable and sealable drug delivery system and Para. [0069] the implanted system contains a drug reservoir and delivery port covered by a permeable layer for release of therapeutic agents to a target organ) and a portion of the housing configured to allow passage of a therapeutic agent (Para. [0069] permeable layer for release of therapeutic agents to a target organ), but fail to explicitly disclose the cell chamber configured to retain a plurality of chondrocytes, the cell chamber having a length and a diameter, the length and the diameter each at least about 3 mm, and therapeutic agent produced via chondrocytes. However, Binette et al. teach the use of matrix substrates and biological gels to house genetically altered chondrocytes which produce therapeutic agents for delivery (Binette et al. Para. [0006] biological gels for chondrocytes that produce therapeutic agents) and wherein the gel matrix substrate housing the chondrocyte has a volume of less than 1 milliliter (Para. [0018] volume of gel substrate is preferably less than one milliliter or one cubic centimeter or 10 millimeters cubed). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Carvalho et al. to include a cell chamber configured to retain chondrocytes for producing therapeutic agents and having a length and diameter greater than 3 mm as taught by Binette et al. for the purpose of rehabilitating an internal bodily organ.

Regarding claim 2, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. further disclose the device wherein the housing comprises a rigid material (Para. [0131] device structures are sufficiently rigid to permit hermetic sealing).

Regarding claim 3, Carvalho et al. in view of Binette et al. disclose the device of claim 2. Carvalho et al. further disclose the device wherein the housing further includes at least one semi permeable port configured to allow passage of the therapeutic agent (Para. [0069] structural layer is permeable for therapeutic agent release).

Regarding claim 4, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. disclose the device further comprising a cap removably coupled to an end of the housing (Para. [0069] series of structures in combination allow a hermetic seal).

Regarding claim 5, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. disclose the device further comprising a suture loop coupled to the housing, the suture loop configured to engage the device to a tissue (Para. [0104] sutures to stabilize implant).

Regarding claim 6, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. disclose the device further comprising a radiopaque marker (Para. [0070] device provides sensitizers and radioactive agents to an organ to assist diagnosis and treatment of those structures).

Regarding claim 13, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. disclose the device further comprising a delivery tube in communication with the housing such that the therapeutic agent can be delivered from the cell chamber to a distant location (Para. [0008] reservoir of an implantable device containing a hormone connected a cavity through a tube).

Regarding claim 16, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. disclose the device further comprising an entrance port configured to allow for the introduction of chondrocytes to the cell chamber (Para. [0067] delivery of the drug is controlled through a sealed interface).

Regarding claim 18, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. further disclose the device wherein the housing is at least partially made from a porous material selected from the group consisting of metals, ceramics, and polymers (Para. [0110] device made by molding process and includes a self-sealing rubber).

(Continued in Supplemental Box)

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
Box V

Claims 7-12 lack inventive step under PCT Article 33(3) as being obvious over Carvalho et al. in view of Binette et al. further in view of Cardamone et al.

Regarding claim 7, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. do not disclose the device wherein the housing further includes an expandable chamber, the expandable chamber separated from the cell chamber by a piston element. However, Cardamone et al. teach an implantable device for dispensing an active agent (Cardamone et al. Abstract and Col. 6, Lns. 46-48 device is implantable) including a biocompatible matrix having one or more expandable portions to facilitate optimum dispersion of the agent (Col. 6, Lns. 30-41, expandable layers) and including a piston element to close an element of the implant (Col. 14, Lns. 60-67, plastic piston closes an end of the device). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Carvalho et al. to include an expandable housing portion separated by a piston element as taught by Cardamone et al. for the purpose facilitating optimum dispersion of a therapeutic agent by an implant.

Regarding claim 8, Carvalho et al. in view of Binette et al. further in view of Cardamone et al. disclose the device of claim 7. Carvalho et al. do not disclose the device wherein the expandable chamber houses a water swellable agent configured to supply a force to the piston in response to an input of water. However, Cardamone et al. teach an implantable device for dispensing an active agent (Cardamone et al. Abstract and Col. 6, Lns. 46-48 device is implantable) including a biocompatible matrix having one or more expandable portions to facilitate optimum dispersion of the agent (Cardamone et al. Col. 6, Lns. 30-41, expandable layers) and including a piston element to close an element of the implant (Cardamone et al. Col. 14, Lns. 60-67, plastic piston closes an end of the device) and wherein swellable agent immersed in solution is partially distended to move the piston (Col. 15, Lns. 48-55, swellable agent partially distended to move piston). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Carvalho et al. to include swellable agent configured to move a piston as taught by Cardomone et al. for the purpose facilitating optimum dispersion of a therapeutic agent by an implant.

Regarding claim 9, Carvalho et al. in view of Binette et al. further in view of Cardamone et al. disclose the device of claim 8. Carvalho et al. further disclose the device wherein the expandable chamber further includes a proximal end having an osmotic membrane thereby allowing for the input of water to the expandable chamber (Para. [0069] permeable membrane for implant reservoir).

Regarding claim 10, Carvalho et al. in view of Binette et al. further in view of Cardamone et al. disclose the device of claim 7. Carvalho et al. further disclose the device further comprising an auxiliary fluid chamber positioned between the cell chamber and the expandable chamber, the auxiliary fluid chamber configured to house an auxiliary fluid and the auxiliary fluid chamber separated from the cell chamber via a semi-permeable membrane (Para. [0102] bi-compartmental reservoir can be used to house an auxiliary fluid).

Regarding claim 11, Carvalho et al. in view of Binette et al. further in view of Cardamone et al. disclose the device of claim 7. Carvalho et al. further disclose the device wherein the auxiliary fluid includes cell nutrients (Para. [0070] therapeutic agents provided for cell cultures).

Regarding claim 12, Carvalho et al. in view of Binette et al. further in view of Cardamone et al. disclose the device of claim 10. Carvelho et al. do not disclose the device wherein the auxiliary fluid includes an agent capable of modifying an aspect of chondrocyte performance. However, Binette et al. teach the use of matrix substrates and biological gels to house genetically altered chondrocytes which produce therapeutic agents for delivery (Binette et al. Para. [0006] biological gels for chondrocytes that produce therapeutic agents) including substances capable of modifying chondrocyte performance (Binette et al. Para. [0094] biological gel matrix can contain nutrients to promote chondrocyte proliferation). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Carvalho et al. to include an agent capable of modifying chondrocyte performance as taught by Binette et al. for the purpose of rehabilitating an internal bodily organ.

Claims 14, 15, and 17 lack inventive step under PCT Article 33(3) as being obvious over Carvalho et al. in view of Binette et al. further in view of Fischell.

Regarding claim 14, Carvalho et al. in view of Binette et al. disclose the device of claim 1. Carvalho et al. disclose the device further comprising an auxiliary fluid reservoir in communication with the cell chamber (Para. [0102] bi-compartmental reservoir can be used to house an auxiliary fluid). Carvalho et al. do not disclose the device wherein communication is via a valve, the valve configured to allow or prohibit the introduction of the auxiliary fluid to the cell chamber. However, Fischell teaches an implantable medication infusion system (Fischell Abstract) wherein a valve is used to control communication between a medication reservoir and a pulsatile pump (Fischell Col. 6, Lns. 34-48, valve 26 connects reservoir to pulsatile pump). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Carvalho et al. to include a valve for control of fluid from an implanted chamber as taught by Fischell for the purpose of facilitating selective release of the fluid.

Regarding claim 15, Carvalho et al. in view of Binette et al. further in view of Fischell disclose the device of claim 14. Carvalho et al. do not disclose the device further comprising a pump in communication with the fluid reservoir. However, Fischell teach an implantable medication infusion system (Fischell Abstract) wherein a pump is in fluid communication with a fluid reservoir (Fischell Col. 6, Lns. 34-48, valve 26 connects reservoir to pulsatile pump). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Carvalho et al. to include a pump in communication with a fluid reservoir as taught by Fischell for the purpose of facilitating selective release of a fluid from the implant.

(Continued in next Supplemental Box)

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:
Previous Supplemental Box

Regarding claim 17, Carvalho et al. in view of Binette et al. disclose the device of claim 16. Carvalho et al. do not disclose the device wherein the entrance port is a rubber septum. Fischell teach an implantable medication infusion system (Fischell Abstract) including the use of a rubber septum with an entrance port (Fischell Col. 5, Lns. 3-14, leaks about the self-sealing rubber septum). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Carvalho et al. to include a rubber septum as taught by Fischell for the purpose of sealing a portion of an implant.

Claims 19-22 lack an inventive step under PCT Article 33(3) as being obvious over Binette et al. in view of Carvalho et al.

Regarding claim 19, Binette et al. disclose a delivery device (Para. [0006] delivery of therapeutic agent from genetically altered chondrocytes), comprising a cell chamber configured to retain a plurality of chondrocytes (Para. [0006] biological gels are used as a matrix to house the chondrocytes), the cell chamber further configured to allow for the release of a therapeutic agent produced by the chondrocytes, but fail to disclose the device wherein the cell chamber is sized such that a portion of the chondrocytes are a distance of at least about 1.5 mm from an outer wall of the device. However, Carvalho et al. teach a delivery device (Carvalho et al. Abstract, surgically implanted delivery device for therapeutic agents) comprising a housing having a cell chamber (Carvalho et al. Para. [0067] implantable and sealable drug delivery system and Para. [0069] the implanted system contains a drug reservoir and delivery port covered by a permeable layer for release of therapeutic agents to a target organ) wherein active agents are maintained a distance away from surface structures to avoid premature interaction (Carvalho et al. Para. [0101] reservoir dividided to maintain active agent to prevent interaction before reaching the surface). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Binette et al. to maintain an active ingredient at a distance from a surface structure wall as taught by Carvalho et al. for the purpose of preserving the active agent. Further, it would have been obvious to one of ordinary skill in the art at the time of the invention to maintain the chondrocytes at a distance of 1.5 mm from an outer wall of the device since where the general conditions of the claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art for the purpose of providing an optimal value of distance to preserve the active agent.

Regarding claim 20, Binette et al. disclose a method for delivering a therapeutic agent to a surgical site (Para. [0006] delivery of therapeutic agent from genetically altered chondrocytes), comprising disposing a plurality of chondrocytes into a cell chamber of a delivery device (Para. [0006] biological gels are used as a matrix to house the chondrocytes), the cell chamber configured to retain the chondrocytes (Para. [0006]), and further configured to allow for release of a therapeutic agent produced by the chondrocytes (Para. [0006]), delivering the delivery device to a surgical site (Para. [0009] genetically altered chondrocyte matrix surgically implanted to target site), and delivering the therapeutic agent from the device to the surgical site (Para. [0009] expression of therapeutic agent to treat disorders), but fail to disclose the method wherein the cell chamber sized such that a portion of the chondrocytes are a distance of at least about 1.5 mm from an outer wall of the device. However, Carvalho et al. teach a delivery method (Carvalho et el. Abstract, surgically implanted delivery device for therapeutic agents) comprising a housing having a cell chamber (Carvalho et al. Para. [0067] implantable and sealable drug delivery system and Para. [0069] the implanted system contains a drug reservoir and delivery port covered by a permeable layer for release of therapeutic agents to a target organ) wherein active agents are maintained a distance away from surface structures to avoid premature interaction (Carvalho et al. Para. [0101] reservoir dividided to maintain active agent to prevent interaction before reaching the surface). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Binette et al. to maintain an active ingredient at a distance from a surface structure wall as taught by Carvalho et al. for the purpose of preserving the active agent. Further, it would have been obvious to one of ordinary skill in the art at the time of the invention to maintain the chondrocytes at a distance of 1.5 mm from an outer wall of the device since where the general conditions of the claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art for the purpose of providing an optimal value of distance to preserve the active agent.

Regarding claim 21, Binette et al. in view of Carvalho et al. disclose the method of claim 20. Binette et al. do not disclose the method further comprising the step of suturing the delivery device at the treatment site. However, Carvalho et al. teach a delivery method (Carvalho et al. Abstract, surgically implanted delivery device for therapeutic agents) wherein a delivery device is sutured at a treatment site (Carvalho et al. Para. [0104] sutures are placed about the device at scleral surface). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Binette et al. to include suturing of the device at a treatment site as taught by Carvalho et al. for the purpose of maintaining the implanted device at a desired location.

Regarding claim 22, Binette et al. in view of Carvalho et al. disclose the method of claim 20. Binette et al. further disclose the method including the step of injecting additional chondrocytes into the delivery device (Para. [0064] injection of chondrocytes using known procedures for delivering vectors and injection at target site).

Claims 1-22 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.